

# Pills, Patches, and Shots: Can Hormones Prevent Aging?

e could not survive without hormones. They are among the most common and vital chemical messengers in the body. From head to toe, each moment of life, they signal cells to perform tasks that range from the ordinary to the extraordinary. Among their many roles, hormones help regulate body temperature, blood pressure, and blood sugar levels. In childhood, they help us "grow up." In the teen years, they are the driving force behind puberty. But what influence, if any, the natural decline in some hormones has on the aging process in middle and late life is unclear. Although a few proponents are convinced that hormone supplements can favorably alter the aging process and have advocated their widespread use, the scientific evidence supporting this premise is, for the most part, sketchy.

For more than a decade, the National Institute on Aging (NIA), a component of the federal government's National Institutes of Health, has supported and conducted studies of replenishing hormones and similar substances to find out if they may help reduce frailty and improve function in older people. These studies have focused on hormones known to decline as we grow older:

- Dehydroepiandrosterone (DHEA)
- Growth Hormone
- Melatonin
- Testosterone
- Estrogen

The results from these NIA-sponsored studies and other research projects likely will improve our understanding of the pros and cons of hormone supplementation. Until the results of these studies are compiled, analyzed, and a consensus among scientists is reached, recommendations to use supplemental hormones and hormone-like molecules to influence the

aging process and health problems associated with aging should be viewed with skepticism. It is not yet known, for instance, how much is too much or too little, and when or whether hormone supplements should be taken at all. This fact sheet provides information about what is known so far and what researchers are doing to find out more.

#### What Is A Hormone?

Hormones are powerful chemicals that help keep our bodies working normally.

The term hormone is derived from the Greek word, *hormo*, which means to set in motion. And that's precisely what hormones do in the body. They stimulate, regulate, and control the function of various tissues and organs. Made by specialized groups of cells called glands, hormones are involved in almost every biological process including sexual reproduction, growth, metabolism, and immune function. These glands, including the pituitary, thyroid, adrenals, ovaries, and testes, release various hormones into the body as needed.

Levels of some hormones like parathyroid hormone, which helps regulate calcium levels in the blood and bone, actually increase as a normal part of aging and may be involved in bone loss leading to osteoporosis. But the levels of a number of other hormones, such as testosterone and estrogen, tend to decrease over time. In other cases, the body may fail to make enough of a hormone due to diseases and disorders that can develop at any age. When this occurs, hormone supplements—pills, shots, topical (rub-on) gels, and medicated skin patches—may be prescribed.

Unproven claims that taking hormone supplements can make people feel young again or that they can slow or prevent aging have been "hot" news items for several years. The reality is that no one has yet shown that supplements of these hormones prevent frailty or add years to people's lives. And while some supplements provide health benefits for people with genuine deficiencies of certain hormones, they also can cause harmful side effects. In any case, people who have genuine hormone deficiencies should take them only under a doctor's supervision. More is not necessarily better. The right balance of hormones helps us stay healthy, but the wrong amount might be damaging.

## **Heed the Warnings**

The NIA recognizes that some hormone-like products are available over the counter and may be used without consulting a physician. The Institute discourages individuals from self-medicating with these products for a number of reasons. First, these products are marketed as "dietary supplements", and therefore are not regulated by the Food and Drug Administration in the same way as drugs. This is an important distinction because the requirements for marketing a dietary supplement are very different from those that apply to hormones marketed as drugs. Unlike drug manufacturers, a firm selling dietary supplements doesn't need FDA approval of its products and doesn't need to prove that its products are safe and effective before marketing. Also, there are no specific good manufacturing practice requirements for dietary supplements. Because of these differing standards, hormone-like substances that are sold as dietary supplements may not be as thoroughly studied as drug products, and, therefore, the potential consequences of their use are not well understood or known. In addition, these over-the-counter products may interfere with other medications you are taking.

Therefore, the NIA does not recommend taking any supplement, including DHEA and

melatonin, that is touted an "anti-aging" remedy because no supplement has been proven to serve this purpose. The influence of these supplements on a person's health is unknown, particularly when taken over a long period of time.

So talk to your doctor if you are interested in any form of hormone supplementation. In fact, you might want to show this fact sheet to your doctor to help explain your concerns.

#### **How Hormones Work**

Most hormones are effective in very low concentrations in the bloodstream. Each hormone molecule travels through the blood until it reaches a cell with a receptor that it matches. Then, the hormone molecule latches onto the receptor and sends a signal into the cell. These signals may instruct the cell to multiply, to make proteins or enzymes, or to perform other vital tasks. Some hormones can even stimulate a cell to release other hormones. However, no single hormone affects all cells in the same way. One hormone, for example, may stimulate a cell to perform one task, while the same hormone can have an entirely different influence over another cell. The response of some cells to hormonal stimulation also may change throughout life.

Hormone supplements, particularly if taken without medical supervision, may adversely affect this complex system. These supplements, for instance, may not behave exactly the same way as our own naturally produced hormones behave because the body may process them differently. In addition, natural hormone production isn't constant, so circulating blood levels may vary significantly over a 24-hour period. Hormone supplements can't replicate these fluctuations. As a result, high doses of supplements, whether pills, gels, skin patches, or shots, may result in excessive and unhealthy amounts of hormones in the blood. Hormone supplements also may compound any negative effects caused by hormones naturally produced by the body.

#### **DHEA**

Dehydroepiandrosterone or DHEA is made from cholesterol by the adrenal glands, which sit on top of each kidney. Production of this substance peaks in the mid-20s, and gradually declines with age. What this drop means or how it affects the aging process, if at all, is unclear. In fact, scientists are somewhat mystified by DHEA and have not fully sorted out what it does in the body. However, researchers do know that the body breaks DHEA down into two hormones that are known to affect us in many ways: estrogen and testosterone (see below).

Supplements of DHEA can be bought without a prescription and are sold as "anti-aging remedies." Some proponents of these products claim that DHEA supplements improve energy, strength, and immunity. DHEA is also said to increase muscle and decrease fat. Right now there is no consistent evidence that DHEA supplements do any of these things in people, and there is little scientific evidence to support the use of DHEA as a "rejuvenating" hormone. Although the long-term (over 1 year) effects of DHEA supplements have not been studied, there are early signs that these supplements, even when taken briefly, may have several detrimental effects on the body including liver damage.

In addition, some people's bodies make large amounts of estrogen and testosterone from DHEA, while others make smaller amounts. There is no way to predict who will make more and who will make less. Researchers are concerned that DHEA supplements may cause high levels of estrogen or testosterone in some people. This is important because testosterone may play a role in prostate cancer, and higher levels of estrogen are associated with an increased risk of breast cancer. It is not yet known for certain if supplements of estrogen and testosterone, or supplements of DHEA, also increase the risk of developing these types of cancer. In women, high testosterone levels can cause acne and growth of facial hair.

Overall, the studies that have been done so far do not provide a clear picture of the risks and benefits of DHEA. For example, some studies in older people show that DHEA helps build muscle, but other studies do not. Researchers are working to find more definite answers about DHEA's effects on aging, muscles, and the immune system. In the meantime, people who are thinking about taking supplements of this hormone should understand that its effects are not fully known. Some of these unknown effects might turn out to be harmful.

#### **Growth Hormone**

Human growth hormone (hGH) is made by the pituitary gland, a pea-sized structure located at the base of the brain, and is important for normal development and maintenance of tissues and organs. It is especially important for normal growth in children.

Studies have shown that supplements are helpful to certain people. Sometimes children are unusually short because their bodies do not make hGH. When they take supplements, their growth improves. Young adults who have no pituitary gland (because of surgery for a pituitary tumor, for example) cannot make the hormone and they become obese. When they are given hGH supplements, they lose weight.

Like some other hormones, blood levels of hGH often decrease as people age, but this may not necessarily be bad. At least one epidemiological study, for instance, suggests that people who have high levels of hGH are more apt to die at younger ages than those with lower levels of the hormone. Studies of animals with genetic disorders that suppress growth hormone secretion also suggest that *reduced* growth hormone secretion may prolong survival in some species.

Although there is no conclusive evidence that hGH can prevent aging, some people spend a great deal of money on supplements. These supplements are claimed, by some, to increase muscle, decrease fat, and to boost an individual's stamina and sense of well being. Shots of the hormone can cost more than \$15,000 a year. They are available only by prescription and should be given by a doctor. In any case, people in search of the "fountain of youth" may have a hard time finding a doctor

who will give them shots of hGH because so little is known about the long-term risks and benefits of this controversial treatment. Some dietary supplements, known as human growth hormone releasers, are marketed as a low-cost alternative to hGH shots. But claims that these over-the-counter products retard the aging process are unsubstantiated.

Scientists are conducting studies to find out if hGH can help make older people stronger by building up their muscles and reducing body fat. They are watching their patients very carefully because side effects can be serious in older adults. These include diabetes and pooling of fluid in the skin and other tissues, which may lead to high blood pressure and heart failure. Joint pain and carpal tunnel syndrome also may occur.

For now, there is no convincing evidence hGH supplements will improve the health of those who do not suffer a profound deficiency of this hormone.

#### **Melatonin**

This hormone is made by the pineal gland, a pea-sized structure in the brain. Contrary to the claims of some, secretion of melatonin does not necessarily decrease with age. Instead, a number of factors, including light and many common medications, can affect melatonin secretion in people of any age.

Melatonin supplements can be bought without a prescription. Some people claim that melatonin is an anti-aging remedy, a sleep remedy, and an antioxidant (antioxidants protect against "free radicals," naturally occurring oxygen-related molecules that cause damage to the body). Early test-tube studies suggested that, in large doses, melatonin might be effective against free radicals. However, cells produce antioxidants naturally, and in test-tube experiments, cells reduce the amount they make when they are exposed to additional antioxidants.

Claims that melatonin can slow or reverse aging are very far from proven. Studies of melatonin have been much too limited to support these claims and have focused on animals, not people. Research on sleep shows that melatonin does play a role in our daily sleep/wake cycle, and that supplements can improve sleep in some cases. If melatonin is taken at the wrong time, though, it can disrupt the sleep/wake cycle. Other side effects may include confusion, drowsiness, and headache the next morning. Animal studies suggest that melatonin may cause some blood vessels to constrict, a condition that could be dangerous for people with high blood pressure or other cardiovascular problems.

These side effects are important to keep in mind since the dose of melatonin usually sold in stores — 3 milligrams — can result in amounts in the blood up to 40 times higher than normal. What long-term effects such high concentrations of melatonin may have on the body are still unknown. Until researchers find out more, caution is advised.

#### **Testosterone**

Ask an average man about testosterone, and he might tell you that this hormone helps transform a boy into a man. Or, he might tell you that it has "something" to do with sex drive. Or, if he has read news stories in recent years, he might mention "male menopause," a condition supposedly caused by diminishing testosterone levels in aging men. In reality, there is scant evidence that this controversial condition, also known as "andropause" or "viropause," exists.

Testosterone is indeed a vital sex hormone plays an important role in puberty. But contrary to what some people believe, testosterone isn't exclusively a male hormone. Women produce small amounts of it in their bodies as well. In men, testosterone is produced in the testes, the reproductive glands that also produce sperm. Once it is produced, the hormone is regulated by the pituitary gland.

As men age, their testes often produce somewhat less testosterone than they did during adolescence and early adulthood, when production of this hormone peaks. But it is important to keep in mind that the range of normal testosterone production is vast. So while there are some declines in testosterone production with age, most older men stay well within normal limits, and

the likelihood that a man will ever experience a major shut down of hormone production similar to a woman's menopause, is remote.

In fact, many of the changes that take place in older men often are incorrectly blamed on decreasing testosterone levels. Some men who have erectile difficulty (impotence), for instance, may be tempted to blame this problem on lowered testosterone. However, in the vast majority of cases, erectile difficulties are due to circulatory problems, not low testosterone.

Still, a small percentage of men may be helped by prescription testosterone supplements. These supplements often are prescribed to men whose bodies do not make enough of the hormone—for example, men whose pituitary glands have been destroyed by infections or tumors, or whose testes have been damaged. For these few men who have extreme testosterone deficiencies, supplements in the form of patches, injections, or topical gel may offer substantial benefit. Supplements may help a man with low testosterone levels maintain strong muscles and bones, and increase sex drive. However, what effects testosterone replacement may have in healthy older men without these extreme deficiencies will require more scrutiny.

The NIA is investigating the role of testosterone supplementation in delaying or preventing frailty. Results from preliminary studies involving small groups of men have been inconclusive, and it remains unclear if supplementation of this hormone can sharpen memory or help men maintain stout muscles, sturdy bones, and robust sexual activity.

Many other questions remain about the use of this hormone in late life. It is unclear, for example, whether men who are at the lower end of the normal range of testosterone production would benefit from supplementation. Some investigators are also concerned about the long-term harmful effects that supplemental testosterone might have on the aging body. It is not yet known, for instance, if testosterone supplements increase the risk of prostate cancer, the second leading cause of cancer death among men. In addition, studies suggest that supplementation might trigger excessive red blood cell production in some men. This side effect can thicken blood and increase a man's risk of stroke.

Although some older men who have tried these supplements report feeling "more energetic" or "younger," testosterone supplementation remains a scientifically unproven method for preventing or relieving any physical and psychological changes that men with normal testosterone levels may experience, as they get older. Until more scientifically rigorous studies are conducted, the question of whether the benefits of testosterone replacement outweigh any of its potential negative effects will remain unanswered.

### Estrogen

Unlike other hormones described in this fact sheet, many large, reliable, long-term studies of estrogen and its effects on the body have been conducted. These studies have clearly shown that estrogen provides many important benefits. Based on this research many women are now advised to take supplements of estrogen to relieve the symptoms of menopause.

But estrogen also is a good example of why it is important to wait until researchers have discovered both the benefits and risks of a hormone supplement before it becomes widely used. While many women are helped by estrogen during and after menopause, some are placed at higher risk for certain diseases if they take it. As research yields more information about this carefully studied hormone, it may help clarify who should take estrogen replacement supplements and who should not.

For many women, the helpful effects of estrogen outweigh the possible harmful effects. Estrogen supplements decrease hot flashes and lower the risk for osteoporosis, a bone-thinning disease that often disables older people. Many studies suggest estrogen also lowers risk for heart disease (the number-one killer of women in the United States) in postmenopausal women. Several recent studies, however, showed no protective effect of estrogen against further heart problems or death from heart disease in women who already had heart disease when starting estrogen supplements. Some studies suggest that estrogen may protect against Alzheimer's disease, but this has not yet been proven. However, recent clinical trials of estrogen

replacement in postmenopausal women with mild to moderate symptoms of Alzheimer's disease have not shown any effects. This is an area of active research.

Yet for all of its promise, estrogen supplementation also has raised a number of serious concerns because some harmful effects are more likely to occur in certain women. For example, most women take a hormone called progestin with their estrogen. Women who do not take progestin have a higher risk of cancer of the uterus (unless they have had a hysterectomy). Estrogen supplements also may raise a woman's risk of getting blood clots, which can block blood circulation in arteries.

Considerable evidence suggests that long-term use (more than 5 years) of estrogen supplements slightly increases a woman's risk of developing breast cancer. In addition, studies also have shown that the risk of breast cancer may be greater among women using combination estrogen/progestin, compared to estrogen alone. Both groups of hormone users had a higher risk of breast cancer than non-users. Lean women who used estrogen appeared to be at greater risk than heavier women. The risk increased with longer duration of use, and returned to the risk of non-users 5 or more years after use was stopped.

So the decision whether to take estrogen is *not* a universal "yes." Researchers have studied estrogen for many years. As a result, doctors are better informed about which women are likely to benefit from supplements and about the right doses to prescribe so that the risk of side effects is reduced. But before choosing this treatment, each woman, along with her doctor, should ask herself:

- Is there heart disease in my family?
- Is there breast cancer in my family?
- Have I had blood clots before, or has my doctor told me I am prone to blood clots?

The answers to these questions, and other factors, will help a woman and her physician make an informed choice about the use of supplemental estrogen, based on a realistic assessment of her personal risks and benefits.

Keep in mind that even after many years of reliable studies of estrogen, researchers continue to discover information about the benefits and risks of this hormone. As these new findings emerge, women and their doctors may have to reassess their decisions about estrogen supplements.

## Many Questions, Few Answers

The other hormones described in this fact sheet have not been studied as long or as intensely as estrogen, and researchers are much further away from knowing all of their helpful and harmful side effects. The NIA sponsors many research projects that will reveal more about the risks and benefits of hormone supplements. One goal is to determine whether DHEA, melatonin, and other supplements improve health of older people, have no effect, or are actually harmful.

It is important to remember that these studies may not give immediate or final answers, especially in the case of DHEA, melatonin, and hGH, since research on these supplements is fairly new. For example, some of the studies may simply give researchers more information about what kinds of questions they should ask in their next studies. Research is a step-by-step process, and larger studies may be needed to give more definite answers.

Until more is known about DHEA, melatonin, and hGH, consumers should view them with a good deal of caution—and doubt. Despite what advertisements or stories in the media may claim, hormone supplements have not been proven to prevent aging. Some harmful side effects already have been discovered, and further research may uncover others.

More is known about estrogen and testosterone, and people who are concerned about genuine deficiencies of these hormones should consult with their doctors about supplements. Meanwhile, people who choose to take any hormone supplement without a doctor's supervision should be aware that these supplements appear to have few clear-cut benefits for healthy individuals, and no proven influence on the aging process.